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Original Article

Prospective Comparative Evaluation of Two Doses of Transdermal Fentanyl for Postoperative Analgesia in Abdominal Hysterectomy

Heena Pahuja[1], Rachana Naitam[2], Tilka Ghate[2], Anjali Bhure[3], Shivani Bhojne[4] & Somakshi Sharma[5*]

[1]*Prof., Department of Anaesthesiology, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, MH, India*
[2]*Assoc. Prof., Department of Anaesthesiology, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, MH, India*
[3]*Prof. & HOD, Department of Anaesthesiology, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, MH, India*
[4]*Resident, Department of Anaesthesiology, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, MH, India*
[5]*MBBS, NKP Salve Institute of Medical Sciences and Research Centre, Nagpur, MH, India*

Abstract

Background: Although transdermal fentanyl is well established in chronic pain management, its optimal dosing for acute postoperative analgesia remains uncertain. Abdominal hysterectomy is associated with significant postoperative pain, necessitating effective and sustained analgesic strategies. This study prospectively compared two doses of transdermal fentanyl for postoperative pain control in patients undergoing elective abdominal hysterectomy under spinal anaesthesia.
Methods: In this prospective comparative study, 44 adult female patients received either a 50 mcg/hr or 25 mcg/hr transdermal fentanyl patch applied three hours prior to surgery. All patients underwent standardized spinal anaesthesia and postoperative care. Pain intensity was assessed using the Numerical Rating Scale over 48 hours. Time to first rescue analgesia, total diclofenac consumption, sedation scores, hemodynamic parameters, and adverse effects were recorded.
Results: Pain scores were similar in the immediate postoperative period but were significantly lower in the 50 mcg/hr group from 6 hours onward, with sustained differences up to 48 hours. The higher-dose group demonstrated prolonged time to first rescue analgesia and reduced supplemental analgesic requirement; more than half required no rescue medication. Hemodynamic parameters and sedation profiles were comparable between groups, and no clinically significant opioid-related adverse effects were observed.
Conclusion: The 50 mcg/hr transdermal fentanyl patch provided more sustained postoperative analgesia than the 25 mcg/hr dose without compromising safety. Appropriate dose selection is essential when incorporating transdermal fentanyl into multimodal postoperative pain management.

Keywords: *Transdermal fentanyl, postoperative analgesia, abdominal hysterectomy, spinal anaesthesia, rescue analgesia*

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Introduction

Effective management of postoperative pain is a cornerstone of modern perioperative care, as it directly influences physiological recovery, functional restoration, and overall patient outcomes.[1] Poorly controlled acute pain can provoke sustained sympathetic activation, impair respiratory mechanics, and delay early mobilisation, thereby increasing the risk of complications such as pulmonary dysfunction, thromboembolic events, and prolonged hospitalisation.[2] Beyond these immediate effects, inadequate analgesia may also negatively impact patient satisfaction and contribute to the transition from acute to chronic postsurgical pain, highlighting the importance of reliable and sustained pain control strategies.[3]
Multimodal analgesia has emerged as the standard approach to postoperative pain management, combining agents and techniques with complementary mechanisms to improve analgesic efficacy while minimising adverse effects.[4] Although neuraxial techniques such as epidural analgesia provide effective pain relief following major abdominal surgery, their invasive nature, technical requirements, and contraindications limit their universal applicability.[5] These limitations have encouraged exploration of alternative methods that are less invasive yet capable of delivering continuous and stable analgesia.
Transdermal drug delivery systems represent one such approach, offering sustained systemic drug delivery without the need for repeated dosing or invasive administration. Fentanyl, a highly potent μ-opioid receptor agonist with favourable lipophilicity, is particularly suitable for transdermal administration, allowing gradual absorption and maintenance of consistent plasma concentrations over extended periods.[6,7] This pharmacokinetic profile has made transdermal fentanyl an established modality in chronic pain management, where stable analgesic coverage is essential.

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*Correspondence and requests should be addressed to S.S. via somakshisharmaa@gmail.com

In contrast, its role in the management of acute postoperative pain remains less clearly defined. When applied prior to surgery, the gradual onset of drug release may allow transdermal fentanyl to provide continuous analgesic support during the early postoperative period, potentially reducing fluctuations in pain intensity and the need for supplemental analgesics.[8] Determining the optimal dose in this setting is important to balance adequate analgesia with safety and tolerability.

The present study prospectively evaluated the analgesic effectiveness and safety of two commonly used doses of transdermal fentanyl patches, 25 mcg/hour and 50 mcg/hour, in patients undergoing elective abdominal hysterectomy under spinal anaesthesia. Postoperative pain intensity, time to rescue analgesia, total supplemental analgesic requirement, hemodynamic parameters, sedation levels, and adverse effects were assessed over the first 48 hours following surgery to determine whether dose selection influences postoperative analgesic quality and safety.

Methods

Study Design and Ethical Approval

This prospective comparative study was conducted at a tertiary care teaching hospital after obtaining approval from the Institutional Ethics Committee (IEC No.: 02/2020). The study adhered to the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

A total of 44 adult female patients scheduled for elective abdominal hysterectomy under spinal anaesthesia were included. Patients received transdermal fentanyl patches delivering either 50 mcg/hour or 25 mcg/hour as part of perioperative analgesic management, and outcomes were prospectively assessed and compared between the two groups. Each group consisted of 22 patients. The sample size was determined based on effect size estimates from prior literature, using a two-sided alpha error of 0.01 and statistical power of 99%, which indicated that 22 participants per group would be sufficient to detect a clinically meaningful difference between the groups.[9]

Participant Selection

Inclusion Criteria: Women aged 18 to 60 years, classified as American Society of Anesthesiologists (ASA) physical status I or II, and scheduled for elective abdominal hysterectomy under spinal anaesthesia were eligible. Participants were required to understand the Numerical Rating Scale (NRS) and provide informed consent.

Exclusion Criteria: Patients were excluded if they had known hypersensitivity to fentanyl, local anaesthetics, adhesives, or nonsteroidal anti-inflammatory drugs; chronic opioid use; significant hepatic, renal, cardiovascular, or respiratory disease; skin lesions at the patch application site; contraindications to neuraxial anaesthesia; or a history of severe opioid-related adverse effects. Patients requiring intraoperative sedatives or systemic opioid supplementation, conversion to general anaesthesia, or those who developed intraoperative complications that could affect postoperative pain assessment were excluded from analysis.

Perioperative Analgesic Intervention

Patients received transdermal fentanyl patches delivering either 50 mcg/hour (Group A) or 25 mcg/hour (Group B), applied to a clean, dry, hairless area of the chest or upper arm three hours prior to surgery to allow adequate time for drug absorption. The choice of patch strength was based on perioperative analgesic planning, and patients were followed prospectively to evaluate postoperative analgesic outcomes. Baseline parameters including heart rate, blood pressure, respiratory rate, oxygen saturation (SpO_2), pain score, and sedation level were recorded prior to surgery.

Anaesthetic Technique and Intraoperative Management

All patients followed standard preoperative fasting guidelines. Premedication included intravenous pantoprazole 40 mg and ondansetron 4 mg. Spinal anaesthesia was administered at the L2–L3 or L3–L4 interspace using 3.4 mL of 0.5% hyperbaric bupivacaine under aseptic precautions. Adequate sensory blockade up to the T6 dermatome was confirmed prior to surgical incision.

Standard ASA monitoring, including electrocardiography, non-invasive blood pressure monitoring, pulse oximetry, and respiratory rate monitoring, was maintained throughout the procedure. Hypotension was managed with intravenous fluids and mephentermine as required, while bradycardia was treated with atropine. No intraoperative sedatives or systemic opioids were administered to ensure consistent postoperative pain assessment.

Postoperative Management and Outcome Assessment

All patients received intravenous paracetamol 1 gram every 12 hours as part of multimodal analgesia. Patients were monitored for 48 hours postoperatively. Pain intensity was assessed using the **Numerical Rating Scale**, and sedation was evaluated using the **Ramsay Sedation Score**. Hemodynamic parameters, including heart rate, blood pressure, respiratory rate, and SpO_2, were recorded immediately after surgery and at 30 minutes, 1, 2, 4, 6, 12, 24, 36, and 48 hours postoperatively. **Rescue analgesia** with intravenous diclofenac 75 mg was administered when the pain score exceeded 4 or upon patient request. The time to first rescue analgesia and total rescue analgesic consumption during the postoperative period were recorded. Adverse effects, including nausea, vomiting, pruritus, skin reactions, excessive sedation, and respiratory depression, were monitored and documented throughout the observation period.

Outcome Measures

Primary Outcome: Postoperative pain intensity assessed using the Numerical Rating Scale during the first 48 hours after surgery.

Secondary Outcomes: Time to first rescue analgesia, total rescue analgesic consumption, sedation levels, hemodynamic parameters, and incidence of adverse effects during the postoperative period.

Statistical Analysis

Data were analyzed using STATA version 10.1. Continuous variables were expressed as mean ± standard deviation and compared using independent-samples t-tests. Categorical variables were analyzed using chi-square tests. Statistical significance was set at $p\text{-value} < 0.05$.

Results

Study Population and Baseline Characteristics

A total of 44 patients were included in the final analysis, with 22 patients in each group. All enrolled patients completed the study and were included in the final analysis. No patients were excluded due to protocol deviations or incomplete data.

The demographic and clinical characteristics were comparable between the two groups, with no statistically significant differences observed in age, weight, height, body mass index (BMI), or ASA physical status ($p > 0.05$), indicating baseline homogeneity between groups.

Table 1. Baseline Demographic and Clinical Characteristics			
Variable	**Group 1 (50 mcg/hr) Mean ± SD / n (%)**	**Group 2 (25 mcg/hr) Mean ± SD / n (%)**	**p-value***
Age (years)	43.31 ± 3.84	45.45 ± 4.79	0.10
Weight (kg)	61.86 ± 6.35	59.68 ± 6.57	0.26
Height (cm)	155.59 ± 2.21	155.72 ± 2.34	0.85
BMI (kg/m²)	25.62 ± 2.84	24.72 ± 2.64	0.28
ASA I	16 (72.7%)	15 (68%)	0.37
ASA II	6 (27.3%)	7 (32%)	
**p-value <0.05 was significant*			

Postoperative Pain Scores (NRS)

Postoperative pain scores were consistently lower in the 50 mcg/hr group compared to the 25 mcg/hr group throughout the 48-hour observation period. Statistically significant differences were observed at 6, 12, 24, 36, and 48 hours postoperatively. These findings indicate superior and sustained analgesic efficacy with the 50 mcg/hr transdermal fentanyl patch.

Table 2. Comparison of Mean NRS Scores Over Time			
Time Interval	**Group 1 (50 mcg/hr) Mean ± SD**	**Group 2 (25 mcg/hr) Mean ± SD**	**p-value***
0 min	2.00 ± 0.00	2.00 ± 0.00	0.20
30 min	2.13 ± 0.35	2.22 ± 0.42	0.44
1 hour	2.54 ± 0.59	2.86 ± 0.77	0.12
2 hours	3.36 ± 0.72	3.36 ± 0.65	1.00
4 hours	4.09 ± 0.68	4.31 ± 0.77	0.32
6 hours	4.45 ± 0.80	5.72 ± 1.12	**0.001**
12 hours	3.81 ± 0.39	4.04 ± 0.37	**0.05**
24 hours	3.18 ± 0.50	3.86 ± 0.77	**0.001**
36 hours	2.90 ± 0.52	3.31 ± 0.64	**0.02**
48 hours	2.54 ± 0.50	2.86 ± 0.35	**0.01**
**p-value <0.05 was significant*			

Time to First Rescue Analgesia

Patients receiving the 50 mcg/hr patch demonstrated a significantly longer duration before requiring rescue analgesia compared to the 25 mcg/hr group (p = 0.007). A majority of patients in the higher dose group did not require rescue analgesia during the observation period.

Table 3. Time to First Rescue Analgesia			
Time Interval	**Group 1 (n = 22)**	**Group 2 (n = 22)**	**p-value***
No rescue needed	13 (59.1%)	3 (13.6%)	**0.007**
Within 4 hours	3 (13.6%)	7 (31.8%)	
Within 6 hours	6 (27.3%)	12 (54.6%)	

p-value <0.05 was significant

Total Rescue Analgesic Requirement

Group 2 demonstrated a substantially higher requirement for diclofenac over 48 hours. In contrast, most patients in Group 1 either required no rescue analgesia or only a single dose.

Table 4. Rescue Analgesic Consumption Over 48 Hours

Rescue Analgesia	Group 1 (50 mcg/hr)	Group 2 (25 mcg/hr)	p-value*
No dose	13 patients	3 patients	0.001
Diclofenac 75 mg	9 patients	10 patients	0.001
Diclofenac 150 mg	0 patients	9 patients	0.001

p-value <0.05 was significant

Hemodynamic Parameters and Sedation

Across all monitored intervals, heart rate, systolic and diastolic blood pressure, mean arterial pressure, respiratory rate, and SpO_2 remained comparable between groups ($p > 0.05$).

Sedation levels, as measured using the Ramsay Sedation Score, did not differ significantly and did not impair patient safety or recovery. No patient required airway support or intervention.

Adverse Effects

No cases of respiratory depression, pruritus, skin reactions, or clinically significant sedation were observed in either group. Mild nausea was observed in 2 patients (9.1%) in the 25 mcg/hr group and 1 patient (4.5%) in the 50 mcg/hr group, which was not statistically significant ($p = 0.54$). No vomiting was reported. Both doses of transdermal fentanyl were well tolerated, with no serious adverse events recorded.

Discussion

This prospective comparative evaluation demonstrates that patients receiving the 50 mcg/hr transdermal fentanyl patch experienced superior postoperative analgesia compared to those receiving the 25 mcg/hr patch following abdominal hysterectomy. The difference became clinically evident after the early postoperative phase and remained consistent throughout the 48-hour observation period. In addition to lower pain scores, the higher-dose group showed delayed requirement for rescue analgesia and reduced overall supplemental analgesic consumption.

An important observation is the temporal pattern of analgesia. Pain scores were comparable between groups during the immediate postoperative period, but a clear divergence emerged from six hours onward. This trajectory corresponds with the known pharmacokinetics of transdermal fentanyl, in which therapeutic plasma concentrations are achieved gradually after application.[8,10] Once steady systemic levels are established, the higher-dose system appears to provide more stable and sustained opioid exposure, translating into improved pain control during the period when postoperative inflammatory pain typically intensifies.[11]

The reduced requirement for rescue diclofenac in the 50 mcg/hr group further supports the clinical relevance of this difference. Beyond statistical significance, this finding suggests a meaningful reduction in breakthrough pain episodes. In practical terms, minimizing supplemental analgesic use may reduce fluctuations in analgesic effect and decrease the risk of dose-related adverse effects associated with repeated parenteral administration.[12,13]

The performance of the 25 mcg/hr patch, while providing measurable analgesia, appeared less suited to the intensity of pain associated with major abdominal surgery. Lower-dose transdermal systems are well established in chronic pain management, where opioid requirements are relatively stable.[14] In contrast, acute postoperative pain presents a higher nociceptive burden, and subtherapeutic transdermal dosing may result in earlier breakthrough pain, as reflected by the clustering of rescue analgesia requirements in this group.

Equally important are the safety findings. Hemodynamic parameters and sedation scores remained comparable between groups, and no clinically significant respiratory depression or serious opioid-related adverse effects were observed. The absence of dose-related safety signals suggests that, when applied with appropriate timing and patient selection, the 50 mcg/hr patch can provide enhanced analgesia without compromising physiological stability. This aligns with existing pharmacological understanding that transdermal delivery produces gradual systemic absorption, potentially reducing the peaks and troughs associated with intermittent opioid administration.[15,16]

From a practical perspective, transdermal fentanyl offers certain logistical advantages in postoperative care. It provides continuous analgesic delivery without the need for infusion pumps or repeated injections, which may be beneficial in settings where simplicity and patient comfort are priorities. The present findings suggest that appropriate dose selection is central to realizing these advantages in acute surgical populations.

Several limitations warrant consideration. The study was conducted at a single center with a modest sample size, which may limit generalizability. Although both groups were managed using a standardized anesthetic protocol, the non-randomized comparative design introduces the possibility of unmeasured confounding factors. Additionally, serum fentanyl concentrations were not measured; therefore, pharmacodynamic inferences are based on clinical response rather than biochemical confirmation. Larger multicenter studies would help further clarify optimal dosing strategies for transdermal fentanyl in acute postoperative settings.

Conclusion

In patients undergoing abdominal hysterectomy under spinal anaesthesia, the 50 mcg/hr transdermal fentanyl patch provided more effective and sustained postoperative analgesia than the 25 mcg/hr patch. The higher dose was associated with lower pain scores, delayed need for rescue analgesia, and reduced supplemental analgesic consumption, without evidence of increased sedation, hemodynamic instability, or respiratory compromise.
These findings support the consideration of the 50 mcg/hr transdermal system as a viable component of multimodal postoperative pain management when carefully selected and appropriately monitored. Optimizing dose selection appears to be key to balancing analgesic efficacy with safety in acute surgical pain.

Declarations

Ethical Approval and Consent to Participate: This study was approved by the Institutional Ethics Committee (IEC No.: 02/2020). All participants were informed about the study procedures and provided written consent prior to enrolment. The study was conducted in accordance with institutional guidelines and the principles of the Declaration of Helsinki.
Consent for Publication: Not applicable, as the manuscript does not include identifiable personal data or images.
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